DETAILED ACTION

This application is a 371 (national stage application) of PCT/US03/20451, which claims priority from US Provisional application 60/392,642.

Claims 1-17, 27-43, & 45 are pending.

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-17 & 43, in the reply filed on 05/13/2008 is acknowledged. Claims 18-26 & 44 are canceled as directed to a non-elected invention. Claims 27-42 & 45 are withdrawn as directed to a non-elected invention, but remain eligible for rejoinder if appropriate conditions are met. Restriction requirement is deemed proper and is, therefore, made final.

Applicant's species election of amiodarone for the anti-arrhythmia agent is acknowledged.

Information Disclosure Statement

2. The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other

information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a).

Specification

3. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The term “kit” as claimed in claim 14 (and claim 15 which depends from claim 14) has no support in the specification.

4. The disclosure is objected to because of the following informalities: The first line of the specification should be amended to reflect this case's status as a national stage application of PCT/US03/20451 which claims benefit of US Provisional application 60/392,642. Appropriate correction is requested.

Claim Objections

5. Claim 4 is objected to because of the following informalities: Tocainide and flecainide are repeated in the listing. Further flecainide is misspelled as flecanide in one instance. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites a list of anti-arrhythmic agents. Included in this listing is "isobutilide." Examiner was unable to find this agent in the Merck Index or other resources. Since this agent is of unknown structure, the claim is indefinite. Applicant is invited to clarify what is meant by "isobutilide" by providing a reference to its structure and function.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1-7, 9, 11, & 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Lindemans *et al.* (US Patent number 6,385,491).

Claim 1: Lindemans *et al.* teach an electrode mounting pad composed of hydrogel capable of delivery of an anti-arrhythmic and an anti-inflammatory agent (claim 1(c) & (d), column 3, lines 18-32, and column 14 lines 3-37).

Claim 2: Lindemans *et al.* teach a hydrogel composition which is biocompatible, biodegradable, and water soluble, and the polymers involved are synthetic and covalently reactive macromers (column 7 lines 13-36).

Claims 3-7: Lindemans *et al.* teach that the anti-arrhythmic agent may be the repolarization prolonging agent amiodarone (column 14 lines 18-26).

Claim 9: Lindemans *et al.* teach amiodarone as an anti-arrhythmic agent (column 14 lines 18-26) which is poorly soluble in water (amiodarone solubility in water 0.07g/100mL, Merck Index).

Claim 11: Lindemans *et al.* teach the anti-arrhythmic agents can be encapsulated in microspheres before being suspended in the hydrogel (column 14 lines 57-61).

Claim 43: Lindemans *et al.* teach the anti-inflammatory agent may be dexamethasone (column 14 lines 27-37).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. Claims 1-13, 16, 17, & 43 are rejected under 35 U.S.C. 103(a) as being obvious over Philbrook *et al*. (US Patent number 7,022,343) in view of Lindemans *et al*. (US Patent number 6,385,491) and Perez *et al*. (US Patent number 5,836,313).

The applied reference (Philbrook *et al*.) has a common assignee and two inventors in common with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Applicant claims an adherent hydrogel designed to deliver both anti-arrhythmic and anti-inflammatory agents to the heart.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Philbrook *et al*. (US Patent number 7,022,343) teaches, as a whole, an adherent hydrogel designed to deliver anti-arrhythmic agents to the heart.

Claims 1 & 43: Philbrook *et al*. teach a tissue adherent hydrogel for delivery of an anti-arrhythmic *agent* (column 1, lines 49-67).

Claim 2: Philbrook *et al*. teach a hydrogel composition which is biocompatible, biodegradable, and water soluble, and the polymers involved are synthetic and covalently reactive macromers (column 2 line 57 through column 3 line 4).

Claims 3-7: Philbrook *et al*. teach that the most preferred anti-arrhythmic agent is the repolarization prolonging agent amiodarone (column 10 lines 11-40).

Claim 8: Philbrook *et al*. teach that the physiologically effective level of amiodarone is maintained for at least seven days post-operation (column 14 lines 39-56).

Claim 9: Philbrook *et al*. teach that the type III anti-arrhythmic agents (including amiodarone) are poorly soluble in water (column 10 lines 26-40).

Claim 10: Philbrook *et al*. teach that nanoparticulate precipitation is the preferred formulation for putting amiodarone into the hydrogel (column 10 line 55 through column 11 line 6).

Claim 11: Philbrook *et al*. teach the anti-arrhythmic agents can be encapsulated in microparticles of a degradable polymer before being suspended in the hydrogel (column 11 lines 6-55).

Claim 12: Philbrook *et al*. teach that the hydrogel patches may be polymerized *in vitro* and then adhered to the tissue surface (column 13 lines 11-27).

Claim 13: Philbrook *et al*. teach "in a preferred embodiment, hydrogels that are formed by photopolymerization of a diacrylated polyethyleneglycol macromer containing hydrolysable linkages provide effective delivery of anti-arrhythmic drugs such as amiodarone applied directly to the atrium … to increase the atrial effective refractory period. The hydrolysable linkages are either lactide-trimethylenecarbonate oligomers or trimethylenecarbonate oligomers, that are cleaved by hydrolysis following application, degrading into simple metabolic products that are non-toxic" (column 2 lines 1-12).

Claims 16-17: Philbrook *et al*. teach that "polymers which can be used to increase the viscosity … include: glycosaminoglycans (GAG) such as hyaluronic acid (HA), carboxymethyl cellulose (CMC), dextran, dextran sulfate, and polyvinylpyrrolidone (PVP)." (column 8 lines 28-36)

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

The difference between the instant application and Philbrook *et al*. is that Philbrook *et al*. does not expressly teach adding an anti-inflammatory agent to the hydrogel. This deficiency in Philbrook *et al*. is cured by the teachings of Lindemans *et al*.

Lindemans *et al*. (US Patent number 6,385,491) teaches, as a whole, a method for attaching an electrode to the heart using a hydrogel pad that is capable of delivering medications (abstract).

Claims 1-13, 16, 17, & 43: Lindemans *et al*. teach a cardiac pad containing an anti-inflammatory agent, specifically dexamethasone (column 14 lines 27-37 and claim 11).

Finding of *prima facie* obviousness

Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the anti-arrhythmia-containing hydrogel patch of Philbrook *et al*. with the anti-inflammatory-containing hydrogel patch or Lindemans *et al*. and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Perez *et al*. (US Patent number 5,836,313) teaches that small amounts of hydrogel degradation product can cause and inflammatory response, especially in vascularized parts of the body (column 5 line 55 through column 6 line 11). Therefore, one would be motivated to include an anti-inflammatory agent in the hydrogel, especially when in use on a vascular organ like the heart.

13. Claims 1, 14, & 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Philbrook *et al*. (US Patent number 7,022,343) in view of Lindemans *et al*. (US Patent number 6,385,491) and Perez *et al*. (US Patent number 5,836,313) as applied to claims 1-13, 16, 17, & 43 above, and further in view of Melanson *et al*. (US Patent number 5,749,968).

The limitations of claim 14 as to the composition of claim 1 are met by Philbrook *et al*. and Lindemans *et al*. as outlined *supra*. Claim 14 uses the terms "means for

increasing adhesion" thereby invoking the means-plus-function language of 35 USC 112 6th paragraph. As such the specification discloses a means for increasing adhesion using a layer of reactive monomers between the hydrogel and tissue to which it will adhere (this is the explicit limitation of instant claim 15). Philbrook *et al*. teach that the preferred method of attaching the gels to the tissue surface is to use macromer solutions to adhere the preformed gel to the tissue.

The difference between what is taught by Philbrook *et al*. and the claimed invention is the limitation of a kit.

The deficiency is cured by Melanson *et al*. Melanson *et al*. (US Patent number 5,749,968) teach, as a whole, adhering gels to substrates. Specifically Melanson teaches a kit containing the means to adhere a gel to a substrate (column 12 lines 31-58). One of ordinary skill in the art would be motivated to combine these elements into a kit because Melanson *et al*. teaches that a kit is a convenient way to package the items for use (column 21 lines 31-58).

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

In light of the forgoing discussion, one of ordinary skill in the art would conclude that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher R. Lea whose telephone number is (571)270-5870. The examiner can normally be reached on Monday-Thursday 7:30-5:00 ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on 571-272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Patrick J. Nolan/
Supervisory Patent Examiner, Art Unit 4161

/CRL/
Examiner, Art Unit 4161